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Stephanie Seidman
FISH & RICHARDSON P.C.
12390 El Camino Real
San Diego, CA 92130-2081

| EXAMINER | |
|---|---|
| KELLY, ROBERT M | |

| ART UNIT | PAPER NUMBER |
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| 1633 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/849,664 | SZALAY ET AL. | |
| | Examiner | Art Unit | |
| | Robert M. Kelly | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *33-35,39,45,46,51,52,54,55,64,65,67-72,74,75,77 and 78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-35,39,45,46,51,52,54,55,64,65,67-72,74,75,77 and 78* is/are rejected.

7)☒ Claim(s) *33-35,39,45,46,51,52,54,55,64,65,67-72,74,75,77 and 78* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/12/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/12/07 has been entered.

Claims 33-35, 39, 45, 46, 51, 54, 64, 65, 67-7274, 75, 77, and 78 are amended.

Claims 36-38, 40-44, 47, 53, 56-63, 66, 73, 76, and 79-80 are cancelled.

Claims 33-35, 39, 45, 46, 51, 52, 54, 55, 64, 65, 67-72, 74, 75, 77, and 78 are presently pending and considered.

### *Claim Status, Canceled Claims*

In light of the cancellation of Claims 36-38, 40-44, 47, 53, 56-63, 66, 73, 76, and 79-80, all objections and/or objections to such claims are rendered moot and thus, are withdrawn.

### *Drawings*

In light of Applicant's explanation that Figures 1-7 are black and white photographs, and hence, require no petition, the objections to the drawings are withdrawn.

***Claim Objections***

Claim 33 is objected to for reciting "the bacterium is non-pathogenic or attenuated; ... and the bacterium replicates in the subject". It would appear that these are conflicting statements. If the bacterium replicates, it is a pathogen in the body. However, given the disclosure of the specification, the Artisan would understand that Applicant is claiming that the bacterium is not normally pathogenic to such organism type, which may be achieved by an attenuation of the organism from an otherwise-pathogenic organism (e.g., paragraph 0028 of the Application Publication). Applicant is requested to correct the terminology to more accurately state what is being claimed.

Claims 34-35, 39, 45, 46, 51, 52, 54, 55, 64, 65, 67-72, 74, 75, 77, and 78 are objected to for depending from an objected-to base claim.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33-35, 39, 45, 46, 51, 52, 54, 55, 64, 65, 67-72, 74, 75, 77, and 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 33, 35, 39 each recite, at least once, "wound, wounded tissue, inflammation site or inflamed tissue". Given that these limitations are provided in the alternative, they must have a distinct scope. It is unclear what the distinction is between "wound" and "wounded tissue" and also the distinction between "inflammation site" and "inflamed tissue". A wound is a wound of

tissue, and an inflammation site is inflamed tissue. Hence, the Artisan would not know the scope of what is being claimed.

Claim 34 and 68-70 each recite "inflammation site or inflamed tissue". Again, the distinction is unclear such that Artisan would understand the scope of what is being claimed.

Claims 34-35, 39, 45, 46, 51, 52, 54, 55, 64, 65, 67-72, 74, 75, 77, and 78 are also rejected for depending from a rejected base claim.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 33-35, 39, 45, 46, 51, 52, 54, 55, 64, 65, 67-72, 74, 75, 77, and 78 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 3-19 of copending Application No. 10/516,785, for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because

Applicant's copending Application teaches broadly the cell/microorganism, and methods of diagnosis, and the specification of Application No. 10/516,785 is substantially identical to the present specification, describing the same uses, and while Application No. 10/516,785 may only broadly claim use, the specification then necessarily teaches the same invention claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

It is noted that these rejections remain held in abeyance until either the present claims, or the claims of 10/516,785 are allowed.

***Claim Rejections - 35 USC § 112 – new matter***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments, the rejections of Claims 33-35, 39, 45, 46, 51, 52, 54, 55, 64, 65, 67-72, 74, 75, 77, and 78 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for lacking a nucleic acid capable of inducing a detectable signal are withdrawn.

To wit, Applicant's claims now require the bacteria to carry such nucleic acid.

***Claim Rejections - 35 USC § 112 – New Matter***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments, the rejections of Claims 33-35, 39, 45, 46, 51, 52, 54, 55, 64, 65, 67-72, 74, 75, 77, and 78 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, due to claiming low back pain which is not herniated nucleus pulposis, is withdrawn.

To wit, the claims no longer claim such.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments, the rejections of Claims 33-35, 39, 45, 46, 51, 52, 54, 55, 64, 65, 67-72, 74, 75, 77, and 78 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for claiming the diagnosis of the various disorders, is withdrawn.

To wit, the claims have been amended to encompass what is reasonably determined to be possessed.

***Claim Rejections - 35 USC § 112 – Enablement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments and arguments, and further consideration, the rejections of Claims 33-35, 39, 45, 46, 51, 52, 54, 55, 64, 65, 67-72, 74, 75, 77, and 78 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, are withdrawn. However:

Claims 33-35, 39, 45, 46, 51, 52, 54, 55, 64, 65, 67-72, 74, 75, 77, and 78 are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed methods in general, does not reasonably provide enablement for topical administration or detection of inflammation/wounds in the brain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

As the enablement rejection has been greatly broadened and only encompasses a few small issues, the following new synopsis of the enablement is provided, however, the bases originally provided in the previous official actions may be looked to for more detailed analysis.

The claims are broad for the methods of administration, and for the detection of inflammation/wounds in the brain. (It is specifically noted that the methods of administration encompass topical administration (paragraph 0046 of the Application Publication of this Specification) and detection of such wounds/inflammation in the brain, as the disorder may be treated with drugs that cross the blood-brain-barrier (e.g., paragraph 0044 of the Application Publication of this Specification) and such disorders as Alzheimer's (paragraph 0050 of the Application Publication of this Specification) are taught as being detectable.

With regard to the methods of administration, Topical administration is not reasonably predicted to produce results, as the skin presents an effective barrier against bacterial infection. For Example, Gelfand (1984) American Journal of Medicine, 76(5A): 158-65 (ABSTRACT

ONLY), provides that skin is a barrier which is compromised to allow infection of a wound. Hence, the Artisan recognized that topical administrations would not allow the bacteria to enter the bloodstream and reach the wound/inflamed tissue.

With regard to the blood-brain-barrier, it has long been known that such barrier is tight-junctioning of endothelial cells of the vasculature of the blood system in the brain which disallows such large things as bacteria to enter (Haung, et al. (2000) Microbes and Infection, 2(10): 1237-44, e.g., pp. 1237-38, paragraph bridging). Moreover, in those cases of bacteria which do cross the blood-brain barrier, meningitis is caused (e.g., ABSTRACT), and such inflammation would inherently be detected, and hence, the method would not detect any preexisting condition, or even such disorders as Alzheimer's disease, but instead, would detect its own meningitis.

Lastly, with regard to the withdrawn aspects, it is noted that the Examiner has found that many bacteria may be found in inflamed as well as in wounded tissue, and such, along with the demonstration of three bacteria of separate generas leaves the Examiner without an argument as to why the Artisan would doubt the efficacy of the methods beyond those embodiments presently rejected.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 33-35, 51, 52, 54, 55, and 67-72 rejected under 35 U.S.C. 103(a) as being unpatentable over Fu, et al. (1994) Zhonghua Wai Ke Za Zhi, 32(10): 615-18 (ABSTRACT ONLY) and the Art in general, as evidenced by: Belas, et al. (1982) Science, 218: 791-93; Prasher, et al. (1987) Gene, 111: 229-33; Meighen, et al. (1992) Journal of Bacteriology, 174: 5371-81; US PAT NO 6,217,847 and Welling, et al. (2000) European Journal of Nuclear Medicine: 27(3): 292-301.

As a preliminary note, the Examiner has only very recently found the Fu reference, and was unable to obtain a translation of such article prior to the due date for issuance of this action, and as such, it is quite possible these claims are anticipated by Fu, or that other rejections may be made. However, for the rejections made, the abstract is sufficient, of which an English copy has been attached. The Examiner will forward a copy of its translation by way of communication as soon such is obtained.

Fu teaches that bacterial flora of the gut can contaminate cutaneous burn wounds (of which official notice is taken that burn wounds are accompanied by inflammation), by the detection of such gut flora in the burn wound (ABSTRACT). Fu teaches that the contamination of wounds from the gut flora should be considered [for treatments]. Hence, from this, the Artisan would be motivated to determine which bacteria present in the gut would contaminate wounds.

The other Art, as Applicant has eloquently demonstrated (Response of 9/12/07, pp. 14-16) demonstrates luciferases (Belas), GFP (Prasher), construction of bacterial constructs for expression of transgenes (Meighen), detection of the light-emitting luciferases/GFP (6,217,847), and MRI detections (Welling).

Hence, at the time of invention, the Artisan would be motivated to make bacteria of intestinal origin containing the transgene, and administer such to the organism for detection by light-determining methods to determine which bacteria colonize the various wounds, for considerations in treatment (it is further noted by way of official notice that one such bacteria would be Escherichia coli, as it is well known to be an intestinal flora). Moreover, the Artisan would expect success, as Fu had demonstrated that bacteria of such origin could colonize inflamed wounds, such as burns, and the Art has already fleshed out the detection methods.

***Conclusion***

No Claim is allowed:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert M. Kelly, Ph.D.
Examiner, USPTO, AU 1633
Patents Hoteling Program
Mailbox 2C70, Remsen Building
(571) 272-0729

Robert M. Kelly